REMARKS

Reconsideration of this application in view of the above amendments and following remarks is respectfully requested. Claims 1-16, 19-22, 25-47, 50, 53-56 and 59-84 are now pending. Claims 17-18, 23-24, 48-49, 51-52 and 57-58 have been canceled. Claims 1, 35, 72-73, 76-77 and 79-80 have been amended. Support for the amendments can be found, for example, in paragraphs [0039], [0065] and [0066], and Examples 1-2 of the application as published (*i.e.*, U.S. published Patent Application No. 2004/0235708). Claims 82-84 are new. Support for the new claims can be found, for example, in paragraphs [0067], [0068] and [0073], and Example 4. No new matter is being introduced.

Claim Rejection –Written Description

Claims 1-81 stand rejected under 35 U.S.C. 112, first paragraph, as allegedly failing to comply with the written description requirement. In particular, the Examiner states that "there is no description in the specification for each m and n > 5" and "support is not found for greater than 2 or 3 that is open ended."

In response, Applicants have amended claims 1, 35 and 73 to recite that m is 2, 3 or 4, and n is 2, 3 or 4. The amendments are made to facilitate allowance and without acquiescing to the rejections in the Office Action or prejudice to future prosecution of the previously pending claims in a related application. Regarding support for m or n being 4 (which is greater than 2 or 3), Applicants submit that the specification describes tetra-functionalized (*i.e.*, m or n is 4) synthetic polymers in, for example, paragraphs [0063]-[0066] and Examples 1-2. Accordingly, Applicants submit that the pending claims (as amended) comply with the written description requirement.

Claim Rejection –Enablement

Claims 1-81 also stand rejected under 35 U.S.C. 112, first paragraph for lack of enablement. In particular, the Examiner is of the opinion that "any or a wide representation of soft and hard tissue is capable of being treated" by the claimed method. The Examiner further states that the pharmaceutical art is unpredictable, and "in the absence of a showing of

correlation between augmenting varying types of both soft and hard tissue claimed as capable of being treated by the method of the instant claims, one of ordinary skill in the art is unable to fully predict possible results from the administration of the compounds due to the unpredictability of the role of the disease." Finally, the Examiner asserts that the claims are "extremely broad", such that one skilled in the art "would have to engage in undue experimentation to test which diseases can be treated by the compounds encompassed in [the] instant claims, with no assurance of success."

Applicants respectfully traverse. First, the claimed invention is directed to tissue augmentation (or bulking), which is a process of adding volume, form or shape to the tissue. In particular, the first crosslinkable component and the second crosslinkable component can be administered to the tissue in need of augmentation, whereby the two components rapidly crosslink to form a gel. There is no particular limitation to the type of tissue, any tissue, whether soft or hard, can be augmented in this manner.

Second, the art of tissue augmentation is not unpredictable in the context of the recited subject matter. Although the bulking agents should satisfy safety criteria such as biocompatibility and non-immunogenicity, they need not be pharmacologically active. For example, the claimed process can be used to reduce wrinkles by augmenting the diminishing collagen layer of aging skin. However, the claimed process is not aimed at reversing or slowing the aging process. The above analogy illustrates the point that the tissue augmentation process changes the physical shape and appearance of the tissue without altering the tissue on a cellular level. Accordingly, one skilled in the art can readily predict the result of administrating the crosslinked composition.

Third, one skilled in the art need not engage in undue experimentation to test which disease can be treated because all one needs to do is to identify the tissue that is in need of augmentation (a readily ascertainable condition) and administer the bulking agent to the site of tissue by injection or implantation. Accordingly, Applicants submit that the claimed methods are fully enabled because it is within the knowledge of one skilled in the art to administer the crosslinked composition to ***any*** tissue in need of augmentation.

Finally, pending claims 35-68 are directed to methods of inhibiting surgical adhesion, not tissue augmentation. Applicants note that, by the Office Action dated March 27, 2006, these claims were considered fully enabled. However, Applicants have amended claim 35 in the same manner as in claims 1 and 73 to facilitate allowance and to comply with the requirements of 35 U.S.C. section 112, first paragraph as it pertains to written description and second paragraph as it pertains to definiteness (discussed below).

Claim Rejection – Definiteness

Claims 1-81 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite. The Examiner takes issue with the use of functional language in the claims.

Claims 1, 35 and 73 have been amended to specifically recite the first crosslinkable component and the second crosslinkable component by their respective structure. Applicants submit that the amendments are made to facilitate allowance and without acquiescing to the rejections in the Office Action or prejudice to future prosecution of the previously pending claims in a related application. In particular, the first crosslinkable component is polypeptide or poly(alkylene oxide) having m nucleophilic groups, which are independently selected from amino and thiol groups; whereas the second crosslinkable component is poly(alkylene oxide) having n electrophilic groups selected from succinimidyl ester, succinimidyl carbonate, sulfosuccinimidyl ester, maleimido, epoxy, isocyanato, thioisocyanato, and ethenesulfonyl. Accordingly, the pending claims (as amended) are definite as they positively identify the claimed elements by their structures.

In addition, the Examiner contends that the meaning of "augmenting soft or hard tissue" is not clear. Applicants traverse. The phrase has its plain meaning, *i.e.*, "augmenting" means to add or increase. Further, one skilled in the art would understand the plain meaning of "soft or hard tissue," particularly in view of the examples provided in the specification of the subject application. For example, soft tissue that may be augmented includes sphincter (*e.g.*, urinary, anal, esophageal), rhytids and scars, whereas hard tissue that may be augmented includes bone and cartilaginous tissue. Accordingly, Applicants submit that the plain meaning

of "augmenting soft or hard tissue" is within the knowledge of one skilled in the art, and thus is sufficiently definite to satisfy the second paragraph of §112.

Claim Rejection – 35 U.S.C. 102 or 103

Claims 1-81 stand rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over U.S. Patent No. 5,162,430 to Rhee et al. ("the '430 patent") or U.S. Patent No. 5,308,889 to Rhee et al. ("the '889 patent").

Neither the '430 patent nor the '889 patent anticipates the claimed invention, as amended. The '430 patent and the '889 patent are both directed to a crosslinked composition of a synthetic polymer and naturally occurring collagen and use thereof. In contrast, the claimed invention is directed to methods of augmenting tissue by administering two synthetic crosslinkable components; namely, a polypeptide or a polyalkylene functionalized with multiple amino or thiol group, and polyalkylene oxide functionalized with multiple activated esters (*e.g.*, succinimidyl ester). Accordingly, the pending claims are not anticipated by the cited references.

Further, the pending claims are not obvious in view of the cited references because there is no teaching or suggestion in the cited reference to crosslink two synthetic components. Instead, the cited references chose natural proteins (*e.g.*, collagen) to create a bulking agent that resembles natural tissue in order to lower adverse immunogenic responses. If anything, the cited references teach away from using synthetic crosslinkable components due to concerns for adverse immunogenic response.

In contrast, the claimed invention is directed to completely synthetic crosslinkable components that are rapidly-gelling and non-immunogenic. The physical properties of the resulting gel can be rationally tuned by the molecular weight, density and concentration of each of the synthetic components. Moreover, unlike collagen-based gels, the synthetic gel is not vulnerable to degradation by collagenase. Accordingly, the cited references fail to satisfy a *prima facie* showing of obviousness (or, if shown, is sufficiently rebutted by the above remarks). Applicants therefore request that this ground of rejection be withdrawn as applied to the pending claims.

Lastly, Applicants submit that the claimed process is allowable over the cited references because it is directed to a process of using Applicants' own patented product. Applicants have previously made a similar argument (*see*, Response filed January 29, 2008). The Examiner has not accepted this argument, stating instead that "[t]he patentability of the examined claims is not based on the issued claims of 6,534,591 and each application is examined on its merits and not examined and allowed because claims of parent application are allowed."

According to TRAINING MATERIALS FOR TREATMENT OF PRODUCT AND PROCESS CLAIMS IN LIGHT OF IN RE BROUWER AND IN RE OCHIAI (MPEP Guidelines), a process claim must be fully examined to determine whether the requirements of 35 U.S.C. 101, 102, 103 and 112 have been met. However, the Training Material further states that "if the process claim includes all the limitations of the allowable product, it is unlikely that a rejection over prior art could be made if the prior art were properly cross-referenced..."

U.S. Patent No. 6,534,591 (the '591 patent), the parent of the instant application, contains granted claims directed to a product based on a crosslinked composition formed by two crosslinkable components. Claim 1 of the '591 patent contains language identical to pending claim 1 of the instant application with respect to the composition used for tissue augmentation (prior to amendments made herein that further narrow claim 1). In addition, the '430 patent and the '889 patents cited by the Examiner in the instant application have also been cross-referenced and considered in the '591 patent. Accordingly, Applicants submit that, because the claimed process is directed to using a patented product and contains all the limitations of a product claim already granted in the '591 patent, the claimed process is patentable over the prior art references cited in the '591 patent.

Conclusion

In conclusion, the pending claims (as amended) satisfy the written description requirement and are fully enabled. In addition, the pending claims (as amended) are not anticipated or rendered obvious by the cited references, particularly in view of the fact that the pending claims are directed to processes of using Applicants' own patented product. Thus, the pending claims (as amended) are allowable and a Notice of Allowance is earnestly solicited.

A good faith effort has been made to place this application in condition for allowance. However, should any further issue require attention prior to allowance, the Examiner is requested to contact the undersigned at (206) 622-4900 to resolve the same.

The Director is authorized to charge any additional fees due by way of this Amendment, or credit any overpayment, to our Deposit Account No. 19-1090.

Respectfully submitted,

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